REMARKS

I. Status of the Claims

Reconsideration of the present application is respectfully requested. Claims 1 and 2 are currently amended to remove "naked recombinant" and "within the age of birth to one month." Support for these amendments can be found throughout the specification and in the Examples, on page 12, lines 4-6, and on page 23, lines 18-22. Claims 1-2 remain currently pending. No new matter is added by way of these amendments.

II. Rejections under 35 U.S.C. § 102(b)

Claims 1 and 2 stand rejected as anticipated under 35 U.S.C. § 102(b) over Ali et al. (Infect Immun 1982, 38(2):610-19) and Murphy et al. (J Clin Microbiol 1986, 24(2):197-202). The Examiner maintains that Ali teaches an infant rat model of administration of attenuated virus for immunization. Additionally, the Examiner states that Murphy discloses immunization using inactivated respiratory syncytial virus vaccine. Based on these teachings, the Examiner incorrectly asserts that the claimed invention is anticipated by the cited references. Applicants traverse the rejection and respectfully request consideration.

Applicants respectfully submit that the claimed invention is novel over both the Ali and Murphy references. Ali does not teach the use of DNA or RNA as presently claimed. Rather, Ali's teachings are limited to the use of virulent and attenuated viruses to invoke immune response in virus-infected infant rats. Murphy also fails to teach the use of DNA or RNA as presently claimed, but rather discloses the investigation of formalin-inactivated respiratory syncytial virus (RSV). Both Ali and Murphy use viral particles, which one skilled in the art would recognize are not the same as DNA or RNA. Therefore, the presently claimed invention is not anticipated by the cited art. Accordingly, applicants request the rejection be withdrawn.

III. Rejections under 35 U.S.C. § 103(a)

Claims 1 and 2 stand finally rejected as unpatentable over U.S. Patent No. 5,795,872 (to Ricigliano) and Milagres et al. (*Infect Immun* 1994, 62(10):4419-24). The Examiner relies on Ricigliano for its purported teaching regarding the use of a DNA construct for use in immunization. The Examiner concedes that Ricigliano fails to teach immunization of infants.

However, the Examiner incorrectly relies on Milagres for a teaching of a protein *Neisseria meningitidis* vaccine in children. The Examiner alleges that based on the cited references, one skilled in the art would have known to substitute the DNA vectors in place of the protein vaccines and that the references provide the basis for a showing of a reasonable expectation of success.

Claims 1 and 2 also stand rejected as unpatentable over Fynan et al. (PNAS 1993, 90(24):11478-82) and Milagres. According to the Examiner, Fynan teaches a variety of specific known antigens for use in DNA constructs for immunization. The Examiner concedes that Fynan fails to teach the immunization of infants, but relies on the teaching of Milagres as noted above to arrive at the claimed invention. Applicants traverse these rejections and respectfully request reconsideration.

Applicants submit that it would not have been obvious for one skilled in the art to substitute DNA vectors in place of the protein vaccines taught in the cited art. Applicants submit that the pending claims as amended further define the target population by amending the claims to read, "wherein the infant mammal is immunized within the age of birth to one month". As previously noted, support for these amendments can be found throughout the specification and specifically on page 12, lines 4-6, and on page 23, lines 18-22. At the time of the filing the application, one skilled in the art would not have found it obvious to immunize an infant nor would there have been any reasonable expectation of success to elicit an immune response.

Milagres' study concluded that functional immune responses are age dependent, however, Milagres was not able to determine what the results were for children under the age of 3 months or what the breakdown of results were within each group of the study. Milagres failed to demonstrate that any immune response was even present, let alone successful, in the claimed "infant" population of birth to one month. In fact, this uncertainty for immunization of infants was the state of the art at the time the present application was filed.

Ricigliano and Fynan also fail to provide any concrete evidence or motivation to arrive at the presently claimed invention. As previously presented, Ricigliano is not enabling for any "antigen", rather Ricigliano requires that the DNA construct contain a muscle specific regulatory element of muscle isozyme of creatine kinase with a specific nucleotide sequence. Furthermore, Fynan merely provides a variety of specific antigens for use in DNA constructs for immunization. Neither reference in combination with Milagres demonstrates any reasonably

expectation that effective immunization of infants from birth to one month could be achieved by administration of a nucleic acid encoding the antigenic peptide.

Applicants submit that even today, the Centers for Disease Control does not generally recommend immunizations from birth to one month. In fact, the only recommendation during this time period is to start the immunization process for hepatitis B. (See Tab A). One skilled in the art would recognize that hepatitis B vaccination includes immune globulins to address preexisting infection from the mother. However, the immunization schedule differs from the claimed invention in that the hepatitis B vaccination requires a series of three injections, the first recommended at birth, but subsequent injections at one month and 6 months after the first injection to obtain successful immunization. Therefore, applicants submit that even today, immunization from birth to one month has not been fully appreciated.

Applicants submit that based on the remarks provided above, the claimed invention is not obvious over the cited art. Accordingly, applicants request that the rejections be withdrawn.

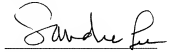
IV. Double Patenting

Claims 1 and 2 stand provisionally rejected under 35 U.S.C. § 101 for double patenting over claims 1-47 of co-pending U.S. patent application serial no. 10/351,630. Applicants note that in the event that claims are allowed in either case, appropriate claim cancellations or amendments will be made in the co-pending application to ensure that they are not coextensive in scope. Since this is a provisional rejection, applicants submit that no such claim amendments are necessary at this time.

V. Conclusion

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,



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TAB A

Recommended Immunization Schedule for Persons Aged 0–6 Years—UNITED STATES • 2007

Vaccine ▼ Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
Hepatitis B[1]	HepB			*see footnote 1*		HepB Series					
Rotavirus[2]			Rota	Rota	Rota						
Diphtheria, Tetanus, Pertussis[3]			DTaP	DTaP	DTaP						
Haemophilus influenzae type b[4]			Hib	Hib	*Hib*[4]				Hib		
Pneumococcal[5]			PCV	PCV	PCV						
Inactivated Poliovirus			IPV	IPV							
Influenza[6]											
Measles, Mumps, Rubella[7]											
Varicella[8]											
Hepatitis A[9]											
Meningococcal[10]											

Range of recommended ages

Catch-up immunization

Certain high-risk groups

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 0–6 years. Additional information is available at http://www.cdc.gov/nip/recs/child-schedule.htm. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at **http://www.vaers.** hhs.**gov** or by telephone, **800-822-7967.**

1. Hepatitis B vaccine (HepB). *(Minimum age: birth)*

At birth:

- Administer monovalent HepB to all newborns before hospital discharge.
- If mother is hepatitis surface antigen (HBsAg)-positive, administer HepB and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth.
- If mother's HBsAg status is unknown, administer HepB within 12 hours of birth. Determine the HBsAg status as soon as possible and if HBsAg-positive, administer HBIG (no later than age 1 week).
- If mother is HBsAg-negative, the birth dose can only be delayed with physician's order and mother's negative HBsAg laboratory report documented in the infant's medical record.

After the birth dose:

- The HepB series should be completed with either monovalent HepB or a combination vaccine containing HepB. The second dose should be administered at age 1–2 months. The final dose should be administered at age ≥24 weeks. Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg after completion of ≥3 doses of a licensed HepB series, at age 9–18 months (generally at the next well-child visit).

4-month dose:

- It is permissible to administer 4 doses of HepB when combination vaccines are administered after the birth dose. If monovalent HepB is used for doses after the birth dose, a dose at age 4 months is not needed.

2. Rotavirus vaccine (Rota). *(Minimum age: 6 weeks)*

- Administer the first dose at age 6–12 weeks. Do not start the series later than age 12 weeks.
- Administer the final dose in the series by age 32 weeks. Do not administer a dose later than age 32 weeks.
- Data on safety and efficacy outside of these age ranges are insufficient.

3. Diphtheria and tatanus toxoids and acellular pertussis vaccine (DTaP). *(Minimum age: 6 weeks)*

- The fourth dose of DTaP may be administered as early as age 12 months, provided 6 months have elapsed since the third dose.
- Administer the final dose in the series at age 4–6 years.

4. *Haemophilus influenzae* type b conjugata vaccina (Hib). *(Minimum age: 6 weeks)*

- If PRP-OMP (PedvaxHIB® or ComVax® [Merck]) is administered at ages 2 and 4 months, a dose at age 6 months is not required.
- TriHiBit® (DTaP/Hib) combination products should not be used for primary immunization but can be used as boosters following any Hib vaccine in children aged ≥12 months.

5. Pneumococcal vaccine. *(Minimum age: 6 weeks for pneumococcal conjugate vaccine [PCV]; 2 years for pneumococcal polysaccharide vaccine [PPV])*

- Administer PCV at ages 2–59 months in certain high-risk groups. Administer PPV to children aged ≥2 years in certain high-risk groups. See *MMWR* 2000;49(No. RR-9):1–35.

6. Influenza vaccine. *(Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 5 years for live, attenuated influenza vaccine [LAIV])*

- All children aged 6–59 months and close contacts of all children aged 0–59 months are recommended to receive influenza vaccine.
- Influenza vaccine is recommended annually for children aged ≥59 months with certain risk factors, health-care workers, and other persons (including household members) in close contact with persons in groups at high risk. See *MMWR* 2006;55(No. RR-10):1–41.
- For healthy persons aged 5–49 years, LAIV may be used as an alternative to TIV.
- Children receiving TIV should receive 0.25 mL if aged 6–35 months or 0.5 mL if aged ≥3 years.
- Children aged <9 years who are receiving influenza vaccine for the first time should receive 2 doses (separated by ≥4 weeks for TIV and ≥6 weeks for LAIV).

7. Measles, mumps, and rubella vaccine (MMR). *(Minimum age: 12 months)*

- Administer the second dose of MMR at age 4–6 years. MMR may be administered before age 4–6 years, provided ≥4 weeks have elapsed since the first dose and both doses are administered at age ≥12 months.

8. Varicella vaccine. *(Minimum age: 12 months)*

- Administer the second dose of varicella vaccine at age 4–6 years. Varicella vaccine may be administered before age 4–6 years, provided that ≥3 months have elapsed since the first dose and both doses are administered at age ≥12 months. If second dose was administered ≥28 days following the first dose, the second dose does not need to be repeated.

9. Hepatitis A vaccine (HepA). *(Minimum age: 12 months)*

- HepA is recommended for all children aged 1 year (i.e., aged 12–23 months). The 2 doses in the series should be administered at least 6 months apart.
- Children not fully vaccinated by age 2 years can be vaccinated at subsequent visits.
- HepA is recommended for certain other groups of children, including in areas where vaccination programs target older children. See *MMWR* 2006;55(No. RR-7):1–23.

10. Meningococcal polysaccharide vaccine (MPSV4). *(Minimum age: 2 years)*

- Administer MPSV4 to children aged 2–10 years with terminal complement deficiencies or anatomic or functional asplenia and certain other high-risk groups. See *MMWR* 2005;54(No. RR-7):1–21.

The Recommended Immunization Schedules for Persons Aged 0–18 Years are approved by the Advisory Committee on Immunization Practices (http://www.cdc.gov/nip/acip), the American Academy of Pediatrics (http://www.aap.org), and the American Academy of Family Physicians (http://www.aafp.org).

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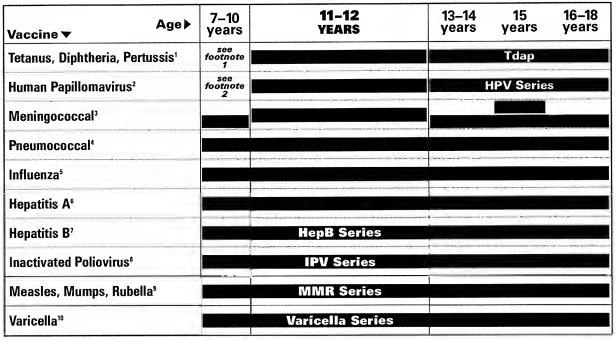
Recommended Immunization Schedule for Persons Aged 7–18 Years—UNITED STATES • 2007



This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 7–18 years. Additional information is available at **http://www.cdc.gov/nip/recs/child-schedule.htm**. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at **http://www.vaers.hhs.gov** or by telephone, **800-822-7967**.

1. Tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap).
(Minimum age: 10 years for BOOSTRIX® and 11 years for ADACEL™)
- Administer at age 11–12 years for those who have completed the recommended childhood DTP/DTaP vaccination series and have not received a tetanus and diphtheria toxoids vaccine (Td) booster dose.
- Adolescents aged 13–18 years who missed the 11–12 year Td/Tdap booster dose should also receive a single dose of Tdap if they have completed the recommended childhood DTP/DTaP vaccination series.

2. Human papillomavirus vaccine (HPV). *(Minimum age: 9 years)*
- Administer the first dose of the HPV vaccine series to females at age 11–12 years.
- Administer the second dose 2 months after the first dose and the third dose 6 months after the first dose.
- Administer the HPV vaccine series to females at age 13–18 years if not previously vaccinated.

3. Meningococcal vaccine. *(Minimum age: 11 years for meningococcal conjugate vaccine [MCV4]; 2 years for meningococcal polysaccharide vaccine [MPSV4])*
- Administer MCV4 at age 11–12 years and to previously unvaccinated adolescents at high school entry (at approximately age 15 years).
- Administer MCV4 to previously unvaccinated college freshmen living in dormitories; MPSV4 is an acceptable alternative.
- Vaccination against invasive meningococcal disease is recommended for children and adolescents aged ≥ 2 years with terminal complement deficiencies or anatomic or functional asplenia and certain other high-risk groups. See *MMWR* 2005;54(No. RR-7):1–21. Use MPSV4 for children aged 2–10 years and MCV4 or MPSV4 for older children.

4. Pneumococcal polysaccharide vaccine (PPV). *(Minimum age: 2 years)*
- Administer for certain high-risk groups. See *MMWR* 1997;46(No. RR-8):1–24, and *MMWR* 2000;49(No. RR-9):1–35.

5. Influenza vaccine. *(Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 5 years for live, attenuated influenza vaccine [LAIV])*
- Influenza vaccine is recommended annually for persons with certain risk factors, health-care workers, and other persons (including household members) in close contact with persons in groups at high risk. See *MMWR* 2006;55 (No. RR-10):1–41.
- For healthy persons aged 5–49 years, LAIV may be used as an alternative to TIV.
- Children aged <9 years who are receiving influenza vaccine for the first time should receive 2 doses (separated by ≥ 4 weeks for TIV and ≥ 6 weeks for LAIV).

6. Hepatitis A vaccine (HepA). *(Minimum age: 12 months)*
- The 2 doses in the series should be administered at least 6 months apart.
- HepA is recommended for certain other groups of children, including in areas where vaccination programs target older children. See *MMWR* 2006;55 (No. RR-7):1–23.

7. Hepatitis B vaccine (HepB). *(Minimum age: birth)*
- Administer the 3-dose series to those who were not previously vaccinated.
- A 2-dose series of Recombivax HB® is licensed for children aged 11–15 years.

8. Inactivated poliovirus vaccine (IPV). *(Minimum age: 6 weeks)*
- For children who received an all-IPV or all-oral poliovirus (OPV) series, a fourth dose is not necessary if the third dose was administered at age ≥ 4 years.
- If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered, regardless of the child's current age.

9. Measles, mumps, and rubella vaccine (MMR). *(Minimum age: 12 months)*
- If not previously vaccinated, administer 2 doses of MMR during any visit, with ≥ 4 weeks between the doses.

10. Varicella vaccine. *(Minimum age: 12 months)*
- Administer 2 doses of varicella vaccine to persons without evidence of immunity.
- Administer 2 doses of varicella vaccine to persons aged <13 years at least 3 months apart. Do not repeat the second dose, if administered ≥ 28 days after the first dose.
- Administer 2 doses of varicella vaccine to persons aged ≥ 13 years at least 4 weeks apart.

The Recommended Immunization Schedules for Persons Aged 0–18 Years are approved by the Advisory Committee on Immunization Practices (http://www.cdc.gov/nip/acip), the American Academy of Pediatrics (http://www.aap.org), and the American Academy of Family Physicians (http://www.aafp.org).

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Catch-up Immunization Schedule for Persons Aged 4 Months–18 Years Who Start Late or Who Are More Than 1 Month Behind

The table below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age.

CATCH-UP SCHEDULE FOR PERSONS AGED 4 MONTHS–6 YEARS					
Hepatitis B[1]	**Birth**	**4 weeks**	**8 weeks** (and 16 weeks after first dose)		
Rotavirus[2]	**6 wks**	**4 weeks**	**4 weeks**		
Diphtheria, Tetanus, Pertussis[3]	**6 wks**	**4 weeks**	**4 weeks**	**6 months**	**6 months**[3]
***Haemophilus influenzae* type b**[4]	**6 wks**	**4 weeks** if first dose administered at age <12 months **8 weeks (as final dose)** if first dose administered at age 12-14 months **No further doses needed** if first dose administered at age ≥15 months	**4 weeks**[4] if current age <12 months **8 weeks (as final dose)**[4] if current age ≥12 months and second dose administered at age <15 months **No further doses needed** if previous dose administered at age ≥15 months	**8 weeks (as final dose)** This dose only necessary for children aged 12 months–5 years who received 3 doses before age 12 months	
Pneumococcal[5]	**6 wks**	**4 weeks** if first dose administered at age <12 months and current age <24 months **8 weeks (as final dose)** if first dose administered at age ≥12 months or current age 24–59 months **No further doses needed** for healthy children if first dose administered at age ≥ 24 months	**4 weeks** if current age <12 months **8 weeks (as final dose)** if current age ≥12 months **No further doses needed** for healthy children if previous dose administered at age ≥ 24 months	**8 weeks (as final dose)** This dose only necessary for children aged 12 months–5 years who received 3 doses before age 12 months	
Inactivated Poliovirus[4]	**6 wks**	**4 weeks**	**4 weeks**	**4 weeks**[4]	
Measles, Mumps, Rubella[7]	**12 mos**	**4 weeks**			
Varicella[8]	**12 mos**	**3 months**			
Hepatitis A[9]	**12 mos**	**6 months**			
CATCH-UP SCHEDULE FOR PERSONS AGED 7–18 YEARS					
Tetanus, Diphtheria/ Tetanus, Diphtheria, Pertussis[10]	**7 yrs**[10]	**4 weeks**	**8 weeks** if first dose administered at age <12 months **6 months** if first dose administered at age ≥12 months	**6 months** if first dose administered at age <12 months	
Human Papillomavirus[11]	**9 yrs**	**4 weeks**	**12 weeks**		
Hepatitis A[9]	**12 mos**	**6 months**			
Hepatitis B[1]	**Birth**	**4 weeks**	**8 weeks** (and 16 weeks after first dose)		
Inactivated Poliovirus[4]	**6 wks**	**4 weeks**	**4 weeks**	**4 weeks**[4]	
Measles, Mumps, Rubella[7]	**12 mos**	**4 weeks**			
Varicella[8]	**12 mos**	**4 weeks** if first dose administered at age ≥13 years **3 months** if first dose administered at age <13 years			

1. Hepatitis B vaccine (HepB). *(Minimum age: birth)*
- Administer the 3-dose series to those who were not previously vaccinated.
- A 2-dose series of Recombivax HB® is licensed for children aged 11–15 years.

2. Rotavirus vaccine (Rota). *(Minimum age: 6 weeks)*
- Do not start the series later than age 12 weeks.
- Administer the final dose in the series by age 32 weeks. Do not administer a dose later than age 32 weeks.
- Data on safety and efficacy outside of these age ranges are insufficient.

3. Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP). *(Minimum age: 6 weeks)*
- The fifth dose is not necessary if the fourth dose was administered at age ≥ 4 years.
- DTaP is not indicated for persons aged ≥ 7 years.

4. *Haemophilus influenzae* type b conjugate vaccine (Hib). *(Minimum age: 6 weeks)*
- Vaccine is not generally recommended for children aged ≥ 5 years.
- If current age <12 months and the first 2 doses were PRP-OMP (PedvaxHIB® or ComVax® [Merck]), the third (and final) dose should be administered at age 12– 15 months and at least 8 weeks after the second dose.
- If first dose was administered at age 7–11 months, administer 2 doses separated by 4 weeks plus a booster at age 12–15 months.

5. Pneumococcal conjugate vaccine (PCV). *(Minimum age: 6 weeks)*
- Vaccine is not generally recommended for children aged ≥ 5 years.

6. Inactivated poliovirus vaccine (IPV). *(Minimum age: 6 weeks)*
- For children who received an all-IPV or all-oral poliovirus (OPV) series, a fourth dose is not necessary if third dose was administered at age ≥ 4 years.
- If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered, regardless of the child's current age.

7. Measles, mumps, and rubella vaccine (MMR). *(Minimum age: 12 months)*
- The second dose of MMR is recommended routinely at age 4–6 years but may be administered earlier if desired.
- If not previously vaccinated, administer 2 doses of MMR during any visit with ≥4 weeks between the doses.

8. Varicella vaccine. *(Minimum age: 12 months)*
- The second dose of varicella vaccine is recommended routinely at age 4–6 years but may be administered earlier if desired.
- Do not repeat the second dose in persons aged <13 years if administered ≥ 28 days after the first dose.

9. Hepatitis A vaccine (HepA). *(Minimum age: 12 months)*
- HepA is recommended for certain groups of children, including in areas where vaccination programs target older children. See *MMWR* 2006;55(No. RR-7):1–23.

10. Tetanus and diphtheria toxoids vaccine (Td) and tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap). *(Minimum ages: 7 years for Td, 10 years for BOOSTRIX®, and 11 years for ADACEL™)*
- Tdap should be substituted for a single dose of Td in the primary catch-up series or as a booster if age appropriate; use Td for other doses.
- A 5-year interval from the last Td dose is encouraged when Tdap is used as a booster dose. A booster (fourth) dose is needed if any of the previous doses were administered at age <12 months. Refer to ACIP recommendations for further information. See *MMWR* 2006;55(No. RR-3).

11. Human papillomavirus vaccine (HPV). *(Minimum age: 9 years)*
- Administer the HPV vaccine series to females at age 13–18 years if not previously vaccinated.

Information about reporting reactions after immunization is available online at **http://www.vaers.hhs.gov** or by telephone via the 24-hour national toll-free information line 800-822-7967. Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for immunization, is available from the National Center for Immunization and Respiratory Diseases at **http://www.cdc.gov/nip/default.htm** or telephone, **800-CDC-INFO (800-232-4636)**.

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